REMARKS

I. Status of Claims

Claims 1-79 were filed with the application, and claims 2, 3, 34, 35, 38, 39, 42, 43, 46, 47, 50, 51, 54, 55 and 67-79 have been canceled. Claims 1, 4-27, 36, 37, 40, 41, 44, 45, 48, 49, 52, 53 and 56-66 are under examination, and claims 28-32 stand withdrawn. Claims 33, 37, 45, 49, 53 and 57-66 are allowed, claims 6-10 are objected to, and the remaining claims are rejected under either or both of 35 U.S.C. §112, first and second paragraphs. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 23 and 24 stand rejected as indefinite under the second paragraph of §112 for use of the term "comprising" in the context of a Markush claim. Applicants have amended the claim as suggested by the examiner, thereby obviating the rejection.

III. Rejection Under 35 U.S.C. §112, First Paragraph

A. Written Description

Claims 22, 23, 36, 40, 44, 48, 52 and 56 stand rejected as allegedly lacking an adequate written description for the use of "retinoids" in combination with CDDO-Me to treat cancer. The examiner argues that there is insufficient disclosure in the specification to define a group of compounds known as "retinoids" that are also cancer chemotherapeutics. As explained below, applicants believe that the term "retinoids" was, at the time of filing, well-known in the field and accepted by the relevant skilled artisan as defining a group of compounds that were useful in cancer therapy. Thus, the rejection is traversed.

Applicants' evidence consists of two review articles, both published prior to the filing of the present application. First, Bollag & Holdener (1992), in their article entitled "Retinoids in Cancer Prevention and Theapy," stated the following:

> ... A correlation between vitamin A and cancer was first noted in the nineteen twenties, when experimentally-induced vitamin A deficiency was shown to lead to hyperplastic, metaplastic and dysplastic tissue changes, *i.e.* preneoplastic lesions and ultimately neoplasms. Forty years later, a preventive effect of vitamin A on the development of chemically-induced tumors was demonstrated in animal models. Further experiments showed that, in addition to its preventive action, vitamin A also had a therapeutic effect in cancer. The antitumor effect was not only associated with vitamin A (retinol) but also with the natural metabolite vitamin A acid (all-trans retinoic acid), as well as other synthetic retinoids. ***This was the basis for the clinical use of retinoids in the prevention and therapy of a variety of precancerous and neoplastic diseases***.

Page 513 (emphasis added; citations omitted). This passage, and in particular the highlighted sentence, reflects the understanding of the field almost a decade before the present application was filed and directly refutes the examiner's argument that one of skill in the art would not believe that applicants were in possession of the genus of anti-cancer retinoids.

Second, applicants point to Dragnev *et al.* (2000), "The Retinoids and Cancer Prevention Mechanisms":

> ... Experimental animal models, cellular models, epidemiological data, and clinical trials provide a strong rationale for the use of retinoids in cancer therapy. Evidence for the retinoid role in cancer was first provided in 1925 ....
>
> ... These and other findings provided a basis for use of retinoids in clinical cancer prevention trials ....
>
> ... These findings, when coupled with the single-agent activity of retinoids in treating overt malignancies, including promyelocytic leukemia, juvenile chronic myelogenous leukemia and mycosis fungoides, and the successful combination therapy with interferon-α-2A in the treatment of squamous cell carcinoma of the skin or cervix and in renal cancer ..., ***provide support for a therapeutic role for the retinoids in the treatment of neoplastic disease***.

Page 362 (emphasis added; citations omitted). As with the first paper, these comments indicate that, at the time the instant application was filed, those in the field understood that the term "retinoids" was appropriately used to describe a class of anti-cancer compounds, and thus arguing against the examiner's position.

In sum, the only ***evidence*** of record on the issue of written description, provided by applicants, clearly shows that the term "retinoids" was synonymous with a family of agents that were understood to have cancer preventative and therapeutic properties. Thus, applicants' use of the term "retinoids" would indeed have been understood by the skilled artisan to mean a genus of compounds generally known to possess anti-cancer properties. As such, written description of this term cannot properly be challenged. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

B. Enablement

Claims 1, 4, 5 and 11-27 stand rejected as lacking enablement for inducing cytotoxicity in other than cancer cells. Applicants traverse, but in the interest of advancing the prosecution, the claims have been amended to recite that the cells being treated are cancer cells. Reconsideration and withdrawal of the rejection is respectfully requested.

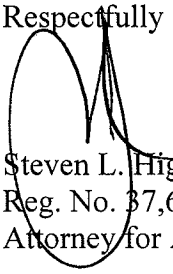
IV. Rejoinder

Applicants believe that as all the claims are in condition for allowance, rejoinder of withdrawn claims 28-32, in light of the relevant linking claim(s), is appropriate at this time.

V. Conclusion

In light of the foregoing, applicants respectfully submit that the withdrawn claims are now eligible for examination and need not be canceled. The examiner is invited to contact the undersigned attorney at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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